

Exhibit E

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

MITSUBISHI TANABE PHARMA
CORPORATION, JANSSEN
PHARMACEUTICALS, INC., JANSSEN
PHARMACEUTICA NV, JANSSEN
RESEARCH AND DEVELOPMENT, LLC,
and CILAG GMBH INTERNATIONAL,

Plaintiffs,

v.

ZYDUS PHARMACEUTICALS (USA)
INC.,

Defendant.

Civil Action No. 17-5005 (consolidated)

**Contains Highly Confidential
Information**

OPENING EXPERT REPORT OF GEERT BEHETS, PH.D.

I, Geert Behets, Ph.D., submit the following report on behalf of Mitsubishi Tanabe Pharma Corp., Janssen Pharmaceuticals, Inc., Janssen Pharmaceutica NV, Janssen Research and Development, LLC, and Cilag GmbH International (collectively, “Plaintiffs”) in this action.

I. EXPERT QUALIFICATIONS

A. Area of Expertise

1. Based on my experience and qualifications, I consider myself an expert in using X-ray diffraction and X-ray fluorescence techniques for crystal identification and localization.

B. Educational Background

2. I obtained a degree in Industrial Engineering – Chemistry with an option in Biochemistry from K.I.H. De Nayer in Belgium in 1992.

3. I received my doctoral degree in Medical Sciences from the University of Leiden in 2005.

C. Relevant Professional Experience

4. I am currently employed by the University of Antwerp as a Senior Scientist in the Pathophysiology Laboratory. I have been employed by the University since 1994. At the start of my employment at the University of Antwerp, I was responsible for developing experimental methods for blood-analysis, mainly in the field of chronic kidney diseases and bone homeostasis. After I obtained my Ph.D., I focused on experimental work in the field of bone biology and the effects of various compounds on bone homeostasis. My work involves basic research as well as pre-clinical work with pharmaceutical companies developing various compounds and treatments.

5. As part my work, I perform, and have performed now for over 20 years, experiments using synchrotron radiation for X-ray fluorescence imaging and X-ray diffraction of

pharmaceutical compounds in collaboration with the European Synchrotron Radiation Facility (“ESRF”) in France.

6. I have also supervised graduate students (at both the Masters and Ph.D. level), post-doctoral researchers, and research scientists with a primary emphasis on basic and pre-clinical research on compounds undergoing development for use in the treatment of renal failure and the prevention of co-morbidities of renal failure. My students’ research often encompasses localizing and analyzing various trace substances in bone samples (both animal and human), and crystal identification.

7. I have consulted widely for industry, particularly in the field of compound development.

8. I am a member of various professional societies, including the American Society of Bone and Mineral Research (ASBMR), the American Society of Nephrology (ASN), and the European Calcified Tissue Society (ECTS).

9. I have published over 50 papers in peer reviewed journals in the field of nephrology, bone metabolism and vascular calcification. I regularly give invited lectures, including keynote and plenary lectures to academics, professional organizations, regulatory bodies, including the FDA, and industry.

10. For a complete list of my professional experiences, publications, and lectures, please see my curriculum vitae attached hereto as Exhibit 1.

D. Compensation

11. I am being compensated at my usual rate of 250 EUR per hour in connection with this proceeding. My compensation does not depend in any way on the outcome of this litigation.

E. Materials Considered

12. A list of materials that I considered for purposes of this report are attached as Exhibit 2. I also relied on my general knowledge, experience, and scientific analysis.

II. OVERVIEW OF WORK PERFORMED

13. I was asked by counsel to perform Synchrotron X-ray diffraction testing on samples of Defendant Zydus Pharmaceuticals (USA), Inc.'s ("Zydus") 100 mg and 300 mg canagliflozin ANDA Products ("Zydus's ANDA Products"). I performed such testing at the European Synchrotron Radiation Facility in Grenoble, France and present the results below.

III. SYNCHROTRON XRD

14. Synchrotron X-ray diffraction (S-XRD) is a technique that uses the diffraction of X-rays on microcrystalline samples for structural and crystal property characterization. A synchrotron is an extremely powerful source of X-rays that are produced by high-energy electrons when their path changes direction due to high intensity magnetic fields. X-rays from the synchrotron irradiate the sample and the sample then diffracts those X-rays. S-XRD measures the way in which the crystalline structure of a compound diffracts the X-rays. That diffraction of X-rays is recorded by a detector which then creates a two dimensional pattern of peaks, called an XRD pattern or diffractogram. Different crystalline forms of a compound diffract X-rays differently, based on the orientation of the molecules within the crystalline structure. Each crystalline form of a compound has its own characteristic XRD pattern, or "fingerprint."

15. S-XRD can therefore be used to identify the crystal structure of a compound and distinguish between different crystalline forms (or "polymorphs") of the same compound. Because the synchrotron produces intense X-rays with high brilliance, S-XRD can be used to

identify and distinguish crystalline forms or identify crystallites at low detection levels (less than a few percent by weight).

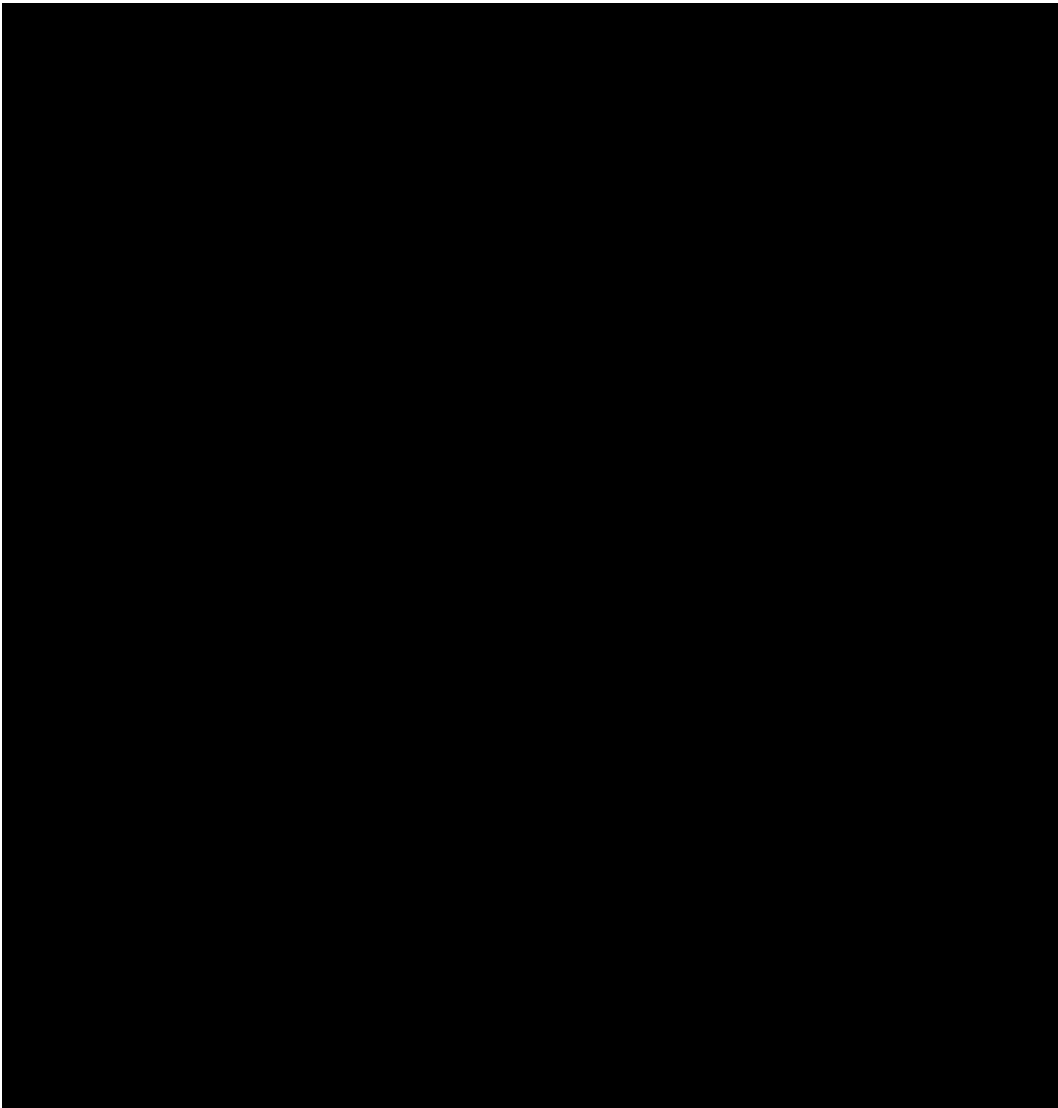
IV. TESTING OF ZYDUS'S ANDA PRODUCTS

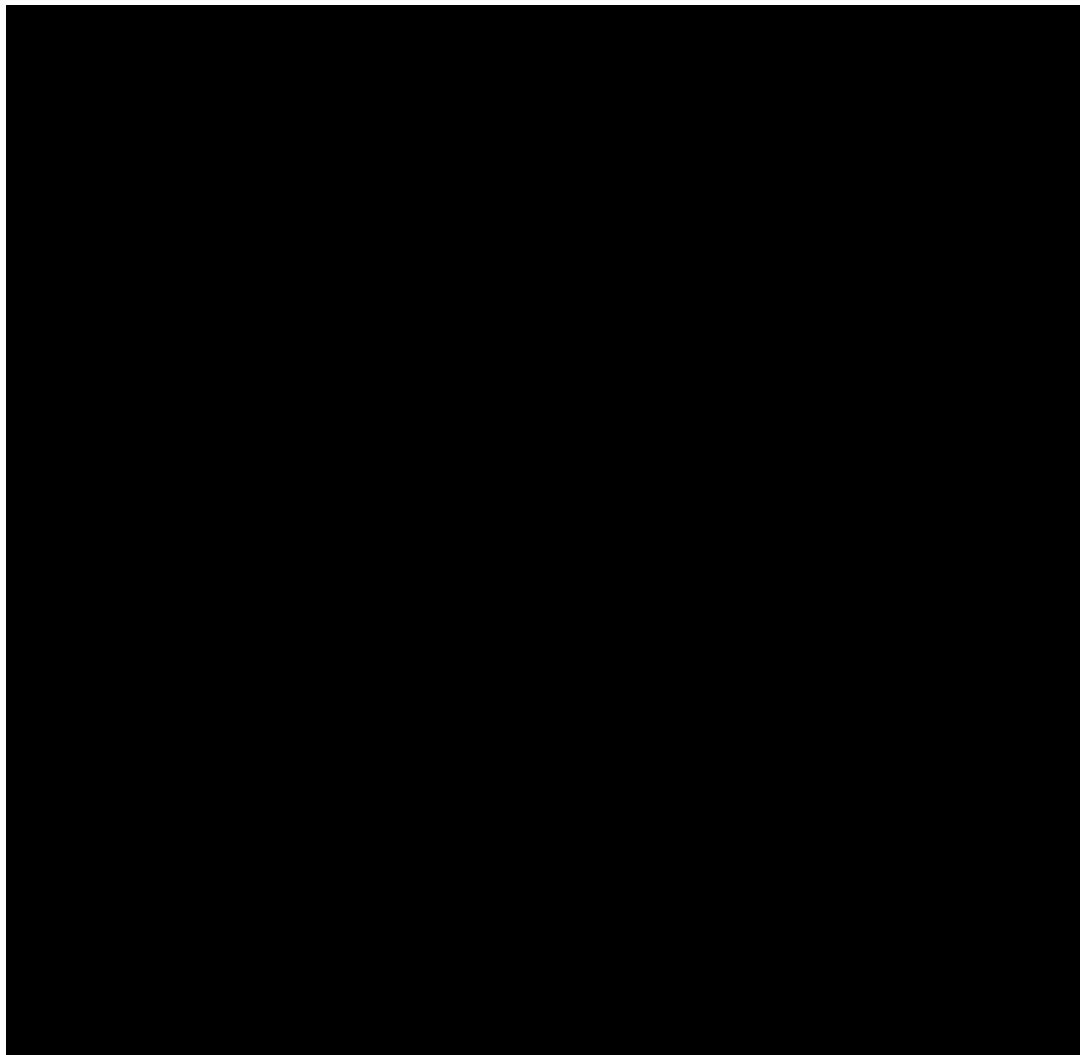
16. I was asked to test samples of Zydus's ANDA Products using S-XRD. In the section below, I provide details related to the samples tested and the methods used.

A. Materials and Methods

1. Samples Tested

17. I conducted testing on the following samples of Zydus's ANDA Products.





18. On August 23, 2018, I received the samples of Zydus's ANDA Products listed in the above table at my laboratory at the University of Antwerp from Karen Gushurst at AMRI SSCI, LLC in West Lafayette, Indiana. (Ex. 3.) The Zydus samples that I received were packaged in bubble wrap inside a Ziplock bag. The Ziploc bag with the samples was in a second larger Ziploc bag containing Drierite inside a Uline insulated container within a FedEx box. The individual dosage strengths of Zydus's ANDA Products were in labeled amber glass vials sealed with screw tops and wrapped in parafilm. I immediately stored the samples at controlled room temperature in accordance with Zydus's directions. (Ex. 4 at ZYDUS-INVOKA 00441530

(“[s]tore canagliflozin tablets at room temperature between 68°F to 77°F (20°C to 25°C)”); *see also* Ex. 5 at ZYDUS-INVOKA 00442002.)

19. Specifically, I stored these tablets as instructed at controlled room temperature in the Laboratory of Pathophysiology of the University of Antwerp. Access to the laboratory is limited to approved persons and requires the use of individual key-cards. I took the unopened Zydus samples with me during my travel to the ESRF, where they were also stored at controlled room temperature in a locked room, until tested. The tablets were removed from their individual packaging just prior to mounting in the S-XRD instrument.

2. Experimental Methods

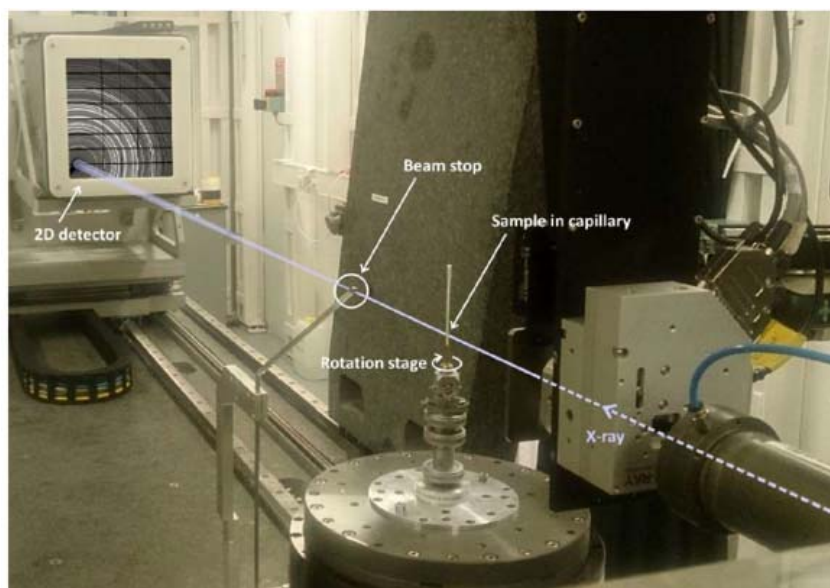
(a) Instrumentation

20. I performed all of the S-XRD measurements at beamline ID15A of the ESRF between August 29, 2018 and August 30, 2018. ID15A is a beamline dedicated and optimized for materials chemistry and materials engineering research. ID15A is used as a source of radiation for diffraction analysis for crystallography research. A ESRF staff member was present at the start of my experiments to ensure the equipment was set up correctly and periodically throughout my experiments provide technical assistance in the event that it was needed. I did not require technical assistance during the course of my experiments.

21. For all of the S-XRD measurements taken of Zydus’s ANDA Products as described in this report, the X-ray energy was set at 50.239 keV, corresponding to an X-ray wavelength of 0.24679 Å and the beam was focused to a spot size of approximately 100 x 100 μm.

(b) Sample Preparation

22. As stated above, the samples of Zydus's ANDA Products were tablets. For each S-XRD measurement, I mounted a single, complete tablet onto a goniometer located on top of a rotation stage. The below photograph illustrates a typical S-XRD setup. Instead of the capillary shown below, however, the entire tablet was mounted onto the goniometer. I then tilted and rotated the tablet to visually align the vertical axis of the tablet with the vertical axis of the rotation stage such that the S-XRD beamline intersected the tablet at the mid-point throughout the rotation.



(c) Data Collection

23. A Dectris Pilatus X 2D detector (2D detector), using a CdTe sensor, was used for data collection. As illustrated above, the 2D detector was positioned approximately 2 meters behind the sample tablet. The 2D detector obtained a 1475 by 1679 pixel diffraction image of each slice of the tablet measured.

24. In the experimental setup, only the part of the tablet directly inside the beam (approx. 100 x 100 μm) is analyzed. In order to measure different areas within each tablet, I first

rotated the sample along its vertical axis at 15 rpm, and took 25 diffraction images each with an integration time of 5 seconds. In this way, I obtained data for one 'slice' of the tablet, perpendicular to its rotation axis. Subsequently, I moved the sample approximately 1 to 2 mm vertically and repeated the previous steps to obtain another image of a new slice. I analyzed each sample at 5 different vertical positions (slices).

(d) Data Reporting

25. In order to report the diffraction images from the 2D detector, I used two customized computer programs developed by the ESRF staff for the S-XRD data generated at the ESRF facility. These programs are routinely used by scientists conducting S-XRD experiments at the ESRF facility to report data in the same manner I did for these experiments. I routinely use these programs when conducting S-XRD experiments.

26. I used one of the computer programs to calculate the median diffraction image for each slice, based on the 25 diffraction images I collected for each the tablet slices. Then, for each sample tablet, I used this program to use the median diffraction images for each slice to calculate an overall median diffraction image for each sample tablet. I also used this program to calculate the median diffraction image of all slices from a tablet sample. I used the second computer program to perform the circular integration of the Debye-Scherrer rings recorded by the detector to create diffractograms. Debye-Scherrer rings are concentric diffraction rings produced by Bragg reflections, which are obtained when the detector is illuminated by the diffracted X-rays.

27. I also used a computer program to convert the S-XRD data to the $\text{CuK}\alpha$ wavelength which is the wavelength used for traditional XRD diffractometers (equivalent to

traditional XRPD data). The computer program uses Bragg's law for the conversion. From Bragg's law:

$$n \lambda = 2d \sin \Theta$$

it can be derived that:

$$\Theta_2 = \sin^{-1} \left(\frac{\lambda_2}{\lambda_1} \sin \Theta_1 \right)$$

whereby λ_1 is the X-ray wavelength used in the S-XRD setup (0.246789 Å), λ_2 is the CuK α wavelength (1.54184 Å), θ_1 is the measured angle in the S-XRD setup and θ_2 is the corresponding angle using traditional diffractometers. This conversion produces the final CuK α diffraction patterns (equivalent to XRPD patterns) for the sample.

(e) Instrument Calibration

28. The instrument geometry was calibrated using a CeO₂ standard. The CeO₂ standard was mounted in the same way as the samples and a diffraction image collected using the same instrument settings. By aligning the obtained rings with the known positions, calibration data such as detector-to-sample distance, vertical and horizontal tilt and beam center position were calculated. These calibration data were subsequently used in all further integrations.

B. Results

29. I have provided the electronic data files associated with the converted CuK α diffraction patterns (equivalent to XRPD patterns) for Zydus's ANDA Products [REDACTED].

V. SUPPLEMENTATION

30. I reserve the right to supplement or amend my report in response to opinions expressed by Zydus's experts, or in light of additional evidence, testimony, discovery, or other information that may be provided to me after the date of this report.

31. In addition, I expect that I may be asked to consider and testify about issues that may be raised by Zydus's fact witnesses and technical experts at trial or in their reports. It may also be necessary for me to supplement my report as a result of ongoing discovery, Court rulings and testimony at trial.

VI. TRIAL EXHIBITS

32. I may rely on visual aids and demonstrative exhibits that demonstrate the bases for my analyses in my report. These visual aids and demonstrative exhibits may include, for example, interrogatory responses, deposition testimony and exhibits, as well as charts, photographs, diagrams, videos, and animated or computer-generated videos.

Executed this 5th day of February 2020, I declare under penalty of perjury that the foregoing is true and correct.



Geert Behets, Ph.D.